EXHIBIT J

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 4 Cases*	

GENERAL EXPERT REPORT OF STANLEY ZASLAU, MD, MBA, FACS

Regarding TVT and TVT-O

This report summarizes my qualifications, training and experience, and my general report opinions about the TVT and TVT-O devices, with a focus on whether the design of the TVT is reasonably safe for its intended use for the treatment of stress urinary incontinence ("SUI"), and the commonly known risks that are associated with incontinence repairs. My opinions are based on the information I have reviewed as of the date of this report. If I receive additional information before trial, I may form additional or modified opinions. All of my opinions are expressed to a reasonable degree of medical and scientific certainty or probability and are based on my education, training, experience, professional society guidelines, analyses, position statements and medical

literature, medical records, the TVT and TVT-O IFUs and Patient Brochures, depositions and other materials I have reviewed, as summarized in the attached reliance list on Exhibit A. Exhibits that may be used to illustrate and support my findings are referenced herein and/or included in the literature and documents from my attached reliance list.

A copy of my CV, which sets out my training, education, experience, and publications, is attached as Exhibit B. A list of cases in which I have testified at trial or deposition during the last four years is attached as Exhibit C.

I am being compensated for my work in this matter at a rate of $500 an hour. For work required to be turned around in 10 days or less, my rate increases to $750 an hour. I have given depositions and testified at trial as an expert witness within the past four years in the following cases: *Please see attached listing.*

I. Background, Training and Experience

I received my undergraduate degree in biology and psychology from Boston University in 1988. I attended Hahnemann University School of Medicine and received my MD degree in 1994. I completed my internship in general surgery and urology residency training at Mount Sinai Medical Center (New York) in 2000. I completed an additional year of training as part of the Consortium Group Urologic Surgical Associates in Brooklyn, New York, where I received advanced training in incontinence, voiding dysfunction, prosthetics and pelvic prolapse.

Upon completion of training in 2001, I accepted a position as Assistant Professor of Urology at West Virginia University. My practice area of focus was

incontinence and voiding dysfunction. I achieved board certification in urology in 2003. I was promoted to Urology Residency Program Director and Associate Professor of Urology in 2005. I was promoted to Professor and Chief of the Division of Urology in 2010.

In 2013, I took and passed the inaugural subspecialty certification examination in Female Pelvic Medicine and Reconstructive Surgery and was the first such certified professional in the State of West Virginia. In 2013, I was named as the Associate Chairman of Education and Research for the Department of Surgery. My practice is still very active in incontinence, voiding dysfunction and sexual dysfunction in men and women. I serve as the Co-Director of the West Virginia University Center for Voiding and Sexual Dysfunction.

I am very active in the practice of incontinence, voiding dysfunction and pelvic floor prolapse. I learned to perform the retropubic TVT procedure in residency (1996-2000) and was able to appreciate the ease of performing this procedure. I was also taught how to perform pubovaginal slings and came to appreciate the added morbidity associated with the abdominal approach to harvest fascia for these cases. Vaginal wall suspensions were also commonly performed during that time and their failure rates and complications of suture erosion and extrusion were also well appreciated by me.

During my year of advanced training, I assisted and performed many retropubic TVT procedures without any intraoperative complications and excellent post-operative results.

From 2001 to the present time, I have performed hundreds of synthetic midurethral slings, including TVT, and more commonly the TVT-O. Although the TVT

is still available at our facility, we commonly use the TVT-O procedure because it is efficient, efficacious and has a lower incidence of potential bowel injuries than the traditional retropubic TVT. I still consider the traditional TVT as part of our armamentarium of suburethral sling options for women with stress urinary incontinence. I am very familiar and comfortable with both retropubic and obturator synthetic midurethral sling procedures and have had excellent success with them, consistent with the clinical results in the level 1 published medical literature. I have not had any bowel, bladder or vascular injuries. I am also comfortable and routinely perform pubovaginal slings (autologous and cadaveric fascia) as indicated or as desired by patients. I carefully review with patients preoperatively, postoperatively and at each subsequent office visit all of the commonly known risks and potential complications of pelvic floor surgery including incontinence, recurrence, voiding dysfunction, pain, sexual dysfunction, mesh erosion and extrusion. This has resulted in excellent long term patient satisfaction over 15 years.

II. Summary of Opinions

A summary of my opinions, as set forth in more detail later in this report, is as follows:

- Many women suffer from urinary incontinence, including stress and urge incontinence. Incontinence can be very detrimental to a woman's quality of life.
- There are non-surgical options for the treatment of stress urinary incontinence. However, non-surgical options are not always effective and

many women ultimately seek surgical treatment after first considering or trying non-surgical treatments.

- Surgical options include Burch colposuspension and sling procedures, consisting of either autologous fascia, cadaveric tissue, materials of other biologic origin, or macroporous, monofilament polypropylene. For many patients, surgery is the most effective treatment for stress urinary incontinence.
- Polypropylene mid-urethral slings like the TVT and TVT-O are widely recognized as the standard of care for treating SUI. They have been extensively studied and authoritative professional organization statements and the medical literature endorse and recommend their worldwide use by physicians in clinical practice which reflect their utility to surgeons, extensive safety profile, and usefulness to patients in the overall surgical armamentarium.
- The TVT and TVT-O sling systems are safe and effective as a treatment for SUI and is less invasive than other surgical treatments. My clinical experience using these devices is consistent with the clinical outcomes in the high level medical literature.
- All surgeries have risks, and surgeries for the treatment of SUI are no exception. The main risks associated with sling procedures are taught to surgeons in training, are discussed in medical textbooks and literature, are learned through hands-on training and continuing medical education, are

tested on board examinations, are discussed at professional conferences and are widely reported in the medical literature.

- Pelvic pain, dyspareunia and other pain is frequently found in women of various ages and in the general background populations. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The medical literature and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline.
- Since my arrival at West Virginia University in 2001, a comprehensive educational and training program to teach the medical and surgical aspects of incontinence has been developed and maintained.
- Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction. Population-based studies that pre-date TVT demonstrate that chronic pelvic pain and persistent dyspareunia affect a large percentage of pre- and post-menopausal women.
- Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from

hysterectomy and scarring from prior episiotomy and repair of tears during childbirth.

- Pelvic pain and other pain (inguinal and lower extremity related pain) are known risks of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures. Pain, sexual dysfunction, dyspareunia, and voiding problems are complications associated with any pelvic floor procedure, including MMK procedures, vaginal or abdominal hysterectomies, bilateral salpingo-oopherectomies, and anterior and posterior repairs.
- Erosions and exposures associated with TVT are rare and can often be treated conservatively. The risks of erosion and exposure were well-known among pelvic floor surgeons since the inception with the original TVT in 1998.
- The polypropylene used in TVT and other synthetic midurethral slings is not cytotoxic.
- TVT and other midurethral slings are not carcinogenic, as suggested by plaintiffs' experts who rely on OHSA Material Safety Data Sheets for raw materials.
- There is no clinically significant distinction between TVT slings using laser-cut mesh and TVT slings using mechanically cut mesh.
- Multiple studies and professional society consensus statements, surveys, and clinical practice guidelines, have confirmed that midurethral synthetic

slings are the treatment of choice and the standard of care for the surgical treatment of SUI.

- The warnings provided in the TVT and TVT-O IFUs appropriately provided pelvic floor surgeons with sufficient information about the potential complications associated with the devices. It is the responsibility of any surgeon to ensure that the patient understands the potential risks and benefits of a procedure. As noted in the IFU, leg pain may occur, but the medical literature and my clinical experience have found persistent leg/groin pain to be rare with the TVT-O. In fact, studies comparing the TVT-O to the TVT-Abbrevo have shown no difference in leg/groin pain after the immediate post-operative period. The professional education provided by Ethicon was comprehensive and well-designed. The vast body of medical literature provides surgeons with the appropriate resource for understanding the frequency and severity of complications associated with TVT, TVT-O, and other pelvic floor procedures, as well as managing complications. The residency and fellowship guidelines require that residents and fellows be familiar with practicing evidence based medicine, counseling patients about potential risks, performing midurethral slings, and become familiar with mesh properties and how to manage complications from SUI procedures.
- Decisions regarding the best treatment for SUI are made by a woman and her doctor.

- Long-term studies evaluating TVT and TVT-O have shown that severe complications are acceptably low and that the TVT and TVT-O are safe and effective procedures for women with SUI.
- As the first subspecialty boarded certified physician in Female Pelvic Medicine and Reconstructive Surgery, I have been able to provide care for, instruction in and surgical training in all aspects of this discipline.
- Instruction on the TVT and TVT-O's indications, procedural specifics and contraindications has been taught to residents in Urology and Ob/Gyn at WVU since my arrival in 2001. This synthetic midurethral sling (both retropubic and transobturator) represents a core treatment for stress urinary incontinence and must be understood by all residents.
- Because the synthetic midurethral sling is considered to be the gold standard, or standard of care treatment for stress urinary incontinence, practicing West Virginia Urologists and Ob/Gyn physicians are not only facile in TVT and TVT-O midurethral sling use, but have routinely performed these procedures since its inception. Didactic knowledge and updates on its use in practice are discussed routinely at state meetings in which I have presented lectures at.
- Residents also receive didactic teaching and surgical instruction in the performance of cadaveric and autologous pubovaginal slings. They come to appreciate the more challenging nature of this procedure and its associated intraoperative and postoperative complications (particularly the significantly increased postoperative pain and voiding dysfunction).

III. Discussion of General Opinions

A. Urinary Incontinence

Urine is produced by the kidneys and flows via peristalsis down the ureter to the bladder. Urine is then held in the bladder until voiding is undertaken. The urethra is at the most distal end of the urinary tract. Urine passes from the bladder through the urethra.

Urinary incontinence occurs when there is an involuntary loss of urine. This condition can be progressive, with significant worsening of symptoms over time. There are several types of urinary incontinence, namely urge incontinence, stress incontinence and mixed incontinence.

Urge incontinence is the involuntary loss of urine associated with increase in bladder pressure. The pressure increases to the point where voiding cannot be deferred and wetting accidents occur. The etiology of urge incontinence can be idiopathic or neurologic and also has significant associations with dietary intake.

Stress urinary incontinence ("SUI") is the sudden involuntary loss of urine in association with exertion, coughing, sneezing or other activity or movement.

If a patient has both urge incontinence and SUI she is described as having **mixed incontinence**.

Many factors have been associated with SUI. Risk factors include obesity, age, parity, vaginal delivery, menopausal status, diabetes, family history and history of hormone replacement therapy. Physical activity and smoking may also be risk factors. SUI may occur with injury or degeneration of the urethral support system or urethral

sphincter mechanism; it is more likely that most women have elements of both problems. Women with a cystocele may have urethral hypermobility but not necessarily stress incontinence. If they have stress incontinence, they may have some urethral sphincter compromise along with the hypermobility.

Trauma from obstetric delivery or another traumatic experience has been implicated in causing stress incontinence. Meyer and colleagues (1998) studied patients during pregnancy and 9 weeks postpartum. They found that 36% of women who were delivered by forceps and 21% who delivered spontaneously suffered from urinary incontinence. Bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. In addition, bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. Women who underwent cesarean delivery were unaffected Levator ani injuries can also occur after childbirth and result in later pelvic floor prolapse.

Stress urinary incontinence is common and is estimated to occur in approximately 1 of 3 women. Dooley and associates (2008) reported that half of women over age 20 complained of incontinence symptoms. In this study, nearly 50% of patients reported pure SUI whereas 34% complained of mixed urinary incontinence. Nyygard and colleagues (2008) and Wu and associates (2010) reported that the prevalence of SUI increases with age. According to an AUA Foundation report in 2011, fewer than 50% of patients who suffer from incontinence report this to their healthcare provider and this may be due to embarrassment and shame. This is very unfortunate, because urinary incontinence can have a profound negative impact on women's well-being. Patients may

experience isolation, limitation of social activities, professional limitations in terms of job advancement/promotion as well as impair intimate relationships. Patients may refrain from beneficial activities such as exercise because of fear of urine leakage. Wu and colleagues (2014) estimated that the lifetime risk for a woman to have surgery to treat SUI is 13.6%. Bing and associates (2015) described clinical risk factors in terms of mixed urinary incontinence, previous incontinence surgery, body mass index greater than 35, age greater than 75, and presence of diabetes as significantly related to a less successful outcome of incontinence surgery.

The AUA guidelines were initially created in 1997 and revised in 2005, 2009 and 2012 to assist clinicians in the diagnosis and treatment of stress incontinence. The guidelines also suggest the importance of diagnosing concomitant pelvic prolapse as this can influence the modality of treatment selected for each patient. Evaluation and symptoms assessment must be undertaken for each patient including demonstration of incontinence with increasing abdominal pressure, frequency of urination, the severity of symptoms and degree of bother, the function of the urethral sphincter and the degree of hypermobility. Each patient should have a focused history to ascertain the type of incontinence present as well as the frequency bother, severity of symptoms and impact of symptoms on lifestyle. Further discussion should focus on the patient expectations of treatment. Physical examination with objective demonstration of stress urinary incontinence is mandatory. Formal urodynamic evaluation may be of assistance in patients with complex presentations of incontinence such as the patient with mixed urinary incontinence. Patients must be counseled about comorbidities that can affect treatment outcomes. This allows the physician to plan an individualized treatment plan,

obtain an informed consent, project an estimate for a successful outcome and list potential complications.

A. Treatment Options for Stress Urinary Incontinence

Once diagnosed, the options for treatment of SUI include behavioral therapy or lifestyle changes, nonsurgical treatment and surgical treatment.

Behavioral therapies include bladder training, fluid and diet management, smoking cessation, weight loss, avoiding bladder irritants and scheduled toilet trips.

Nonsurgical options include Kegel exercises and the use of a pessary (a device inserted into the vagina to support the pelvic area and urethra). Kegel exercises are patient-taught exercises to identify the muscles of the pelvic floor that are involved in maintaining urinary continence. Patients are taught to squeeze and relax these muscles several times each hour, several times per day. When conducted over the long term, patients can see a modest improvement in urinary incontinence symptoms. However, success with Kegel exercises requires a motivated patient. Thus, there is a significant drop out rate for this therapy and many patients will go on to require additional therapies. (Laners 2011).

Pessaries are silicon, non-allergic devices that are placed into the vaginal canal to reduce pelvic floor prolapse. In general, these are used in patients with pelvic floor prolapse. Some patients with prolapse also complain of urinary incontinence. Pessaries can be considered for these patients. There is no difference between the types of pessary used when looking at patient satisfaction with this therapy. Pessaries need to be removed periodically to be cleaned and are then replaced. Many patients with pessaries drop out from this therapy because it is cumbersome and requires quite a bit of follow up care.

The index patient to consider a pessary for is one with significant pelvic floor prolapse who is a poor surgical risk because of multiple medical problems. It is most successful in the elderly patient. (Clemens 2004; Brincat 2004; Mutone 2004).

Usually, nonsurgical or behavioral options are helpful only in milder cases of urinary incontinence, and only provide a lasting cure in a small subset of patients. For example, while many women experience some improvement from Kegel exercises, in my clinical experience few find this to be a permanent solution. Similarly, pessaries are not convenient and can lead to vaginal discharge, pain, odor or bleeding. Many women discontinue pessaries or other similar nonsurgical treatments. Dropout rates can be as high as 60% in the short term. (Powers 2004; Sarna 2009).

Biofeedback with pelvic floor muscle therapy teaches patients to identify muscles in the pelvic floor that are responsible for bladder and bowel continence. Through identification of these muscles, patients learn to control muscle function and possibly improve continence. This modality requires periodic therapy visits lasting approximately 30 minutes in duration for a several week cycle. Some improvement in urinary incontinence is noted for the motivated patient in the short term. Biofeedback can also be combined with electrostimulation of the pelvic floor muscles and short-term studies show limited benefit through this additive therapy. However, with biofeedback (with or without electrostimulation), there is a significant dropout rate from treatment and many patients will go on to other therapies. (Diaz 1997; Susset 1995; Weinberger 1999).

Bulking agents like collagen are sometimes used to treat SUI. In this treatment, the agent is injected into the periurethral tissues around the bladder neck via the cystoscope. Success rates are approximately 34% at 12 months with 26% of patients

having no improvements at all from this therapy. This is not a permanent repair and is not as effective as surgery. (Diaz 1997).

B. Surgical Treatment Options Prior to TVT

Surgery is the most effective and definitive way to treat SUI. Surgical options include colposuspension and sling procedures consisting of either rectus fascia or fascia lata from the patient, cadaveric or biologic tissue, and macroporous, monofilament polypropylene used in the TVT.

Prior to the TVT, the most popular surgery to treat SUI was the Burch colposuspension. The Burch colposuspension is an invasive surgical procedure involving an abdominal incision and identification of the pelvic bony ligamentous structures. Sutures are placed into the periurethral tissue and into the bony ligamentous structures. The long-term success rate for the Burch procedure is approximately 50-60%. (Albo 2007; Feyeresil 1994; Abu-Heija 1994). Galloway (1987) reported their experience with Burch procedures. Continence was achieved in only 42 patients (approximately 50% of all patients). Although all but one patient without previous surgery became continent, only 12 of 19 patients who had undergone previous surgery were continent post-operatively and five of the seven who showed little or no improvement had had at least two previous procedures for incontinence. They reported an unacceptable number of post-procedural complications including: persistent incontinence, voiding difficulties, urge syndrome, post-colposuspension syndrome, uterine prolapse, enterocele, dyspareunia, and recurrent incontinence. Demirci (1991) studied the long-term complications of Burch procedures. They noted, at follow up, late complications

occurred in 220 women. These included cystocele in 18; rectocele in 32; enterocele in 35; dyspareunia in 6, and groin or suprapubic pain in 15. They noted that the cure rate of Burch colposuspension is satisfactory, although it declines with time. Alacay (1995) reported their long-term complications from Burch procedures. They noted post-operative complications including de novo detrusor instability in 15% of patients, long term voiding difficulty in 22% of patients and recurrent UTI in nearly 5% of patients.

Kjolhede (1996) studied the rate of prolapse after Burch procedures. They found on clinical examination a significant progression of rectoceles ($p=0.003$) after the colposuspension. Six women (29%) had subsequent corrective prolapse surgery within 2 years after the colposuspension. Parisio (2004) compared TVT to laparoscopic Burch procedures for stress urinary incontinence. They noted post operative symptoms of incontinence (stress, urge, and any urinary incontinence) were reported significantly more often in the laparoscopic Burch colposuspension group that in the TVT group. Kayan (2008) studied the effects of sexual function after Burch procedures when compared to vaginal slings. They noted that postoperative sexual function improved in 13 women (24.5%) of the vaginal sling group and in 5 women (12.2%) of the Burch colposuspension group, and remained unchanged in 15 (28.3%) and 10 (24.4%), respectively. Sexual function deteriorated in 25 (47.2%) of the sling group and 26 (63.4%) of the Burch group. They concluded that sexual function may be impaired after surgery for SUI. Burch colposuspension may deteriorate sexual function much more than vaginal sling surgery in women. Therefore, women who will need surgery for SUI should be informed of the risk of deterioration of sexual function after surgery.

Geller and colleagues (2013) described the dramatic shift over the past two decades as the synthetic midurethral sling has replaced the fascial sling and Burch colposuspension as the criterion standard for treatment of female stress urinary incontinence.

Albo and colleagues (2007) studied two groups of patients with SUI. They noted a success rate of 49% for Burch and 66% for fascial slings in patients with SUI. They noted that more women who had a fascial sling had UTIs, difficulty voiding and post-op urge incontinence. The rate of voiding dysfunction after these procedures ranges from 2% to 20%. (Rodrigues 2004). Additionally, erosions of autologous fascial slings has been reported. (Handa 1999; Webster 2003; Golumb 2001). The Burch procedure because of its abdominal incision, usually requires an inpatient hospital stay and has complications of wound infection, urethral injury and voiding dysfunction. As discussed below, the TVT has become much more popular than the Burch procedure and fascial sling because of its high efficacy, low morbidity, less invasiveness and ease of use.

Other types of surgical procedures used in the past to treat SUI, such as the Marshall-Marchetti-Krantz procedure, anterior colporrhaphy and needle suspension procedures, are not used very often today and are not recommended as the standard of care by medical associations because of a lack of efficacy and/or their complication profiles. (Ostergard in Pelvic Floor Dysfunction, 6th Edition 2008, pg. 226-7).

C. Reasonableness of the TVT and TVT-O's Design for its Intended Use and its Utility / Usefulness

TVT was initially introduced in 1998 as a minimally invasive way to treat SUI. This was needed because of the surgical challenges with Burch and Pubovaginal

slings discussed above. Further, there were significant complications and lack of efficacy seen with needle suspension procedures (Raz Bladder Neck Suspension, Pledget-based needle suspensions and the four cornered vaginal sling). While short term (6-12 month) success was common with these procedures, longer term success was lacking. Further, there were significant complications noted with some of the procedures (Pledget-based needle suspensions) including erosion into the urethra and bladder. Thus, the need to invent a minimally invasive procedure was warranted. The TVT fulfilled this need by being minimally invasive and is easy to perform when indicated and when the guidelines specified by the manufacturers are followed accordingly. Patients certainly wanted a minimally invasive procedure that could treat their stress urinary incontinence and have them able to resume their usual daily activities with a short recovery period and periodic follow up with their physician to ensure that they were doing well.

The design is safe and the short/long term efficacy is certainly present. To date, I have never had injury to any nerve, bowel or bladder (other than incidental isolated recognized trocar injury to the bladder, easily treated with short term catheter placement). TVT-O, which uses the same Prolene mesh as TVT, became available in 2004 as another tool in surgeons' toolkits to help treat incontinence with a reduced risk of perforating the bladder. In my experience I have had 3 cases of TVT mesh extrusion treated only with simple excision. My success rates are excellent and go out to 15 years with the use of TVT and TVT-O procedures with most patients dry or still significantly improved from pre-operative baseline.

TVT and TVT-O implantation are both technically easy to perform and easy to teach. The tape is fashioned under the urethra using small standard vaginal wall

dissection that is only 1.5cm in length. This design involves minimal dissection to create a small tunnel for the sling to be placed into which follows the path of the urethropelvic ligament. As compared to the traditional pubovaginal sling, this dissection is quicker and easier to perform.

Explicit instructions via video and step by step instructions were provided by the manufacturer. Professional education courses were also provided by the manufacturer on how to safely perform this procedure. When I learned how to perform this procedure in residency, I viewed the videos, which carefully explained all the necessary steps of the procedure.

Emphasis was placed on positioning the tape under the midurethra in a tension free manner using a clamp or Hegar dilator behind the tape so it does not obstruct the urethra. A Babcock clamp can also be used and can be placed around one of the plastic trocars once it has been transected after being positioned and removed from its thigh exit point. This allows the mesh to be positioned at the mid urethra easily. The trocar is placed around the mesh in the midline and the Babcock maintains the position. This prevents the mesh from being placed under tension or stretched. Any of the abovementioned techniques are considered to be a critical portion of the procedure and allows the sling to sit without tension so that over time its incorporation into the tissue planes will be such that it mimics the location of the normal urethropelvic ligament and minimizes urethral hypermobility during stress. This is a critical design feature that physicians who perform the procedure must pay careful attention to in order to limit potential adverse effects such as voiding dysfunction, urethral pain and urethral erosion.

The manufacturer's videos, IFU and subsequent articles by leading academic physicians have further reiterated this concept. Instruction was also provided to slowly remove the plastic sheath to prevent shearing of the tape. This is well illustrated on the manufacturer's videos and subsequent articles by leading academic physicians. It is well known that when the plastic tape is pulled quickly or is under excessive tension that the mesh can lose a few particles from the ends of tape. Such a reaction does not occur when used as designed. The sheath covering the mesh is easily removed when removed as instructed and the techniques described above are utilized to prevent the mesh from being placed under tension. Further, I have not seen any complications attributed to particle loss or mesh fraying in the hundreds of randomized controlled trials evaluating the safety and efficacy of TVT and TVT-O, nor have I had any problems or complications associated with particle loss from TVT or TVT-O in my practice. Likewise, there are no reliable scientific studies evaluating the TVT or TVT-O that have demonstrated any clinical significance to alleged cytotoxicity, degradation, or cancer.

Carcinogenic Potential of Mesh Used in the Treatment of Stress Incontinence

Carcinogenesis has become another point discussed by plaintiffs' experts. King (2014),Moalli (2014), and Linder (2016) reviewed the incidence of malignancy associated with pelvic mesh. No reports of malignancy have been reported in humans directly associated with these slings. The FDA, AUGS, and SUFU all have reported that polypropylene midurethral slings are safe and effective. We all believe that continued research is necessary but should be done in a scientific fashion to ensure its validity. As of this writing, there is no evidence to suggest that polypropylene midurethral slings have

any association with malignancy.

Moalli (2014) reviewed the potential for carcinogenicity with polypropylene mesh in their review article. The authors noted that potential for neoplasm from such implanted mesh has never been shown to be causative. They cited an epidemiologic study by the International Agency for Research on Cancer (2000) that concluded that there was no evidence for tumorigenicity of metallic or synthetic implants in humans. The authors propose that the potential for carcinogenesis of polypropylene mesh is negligible when the low incidence of reports of carcinogenesis is considered given the world wide use of polypropylene as a suture for hernia mesh in millions of patients over the last 50 years. Finally, the authors state the similarity of mesh to the use of breast implants in that millions of women have been treated successfully with no evidence of systemic complications including cancer and haven been able to have significant improvement in their quality of life as a result of their surgery.

Linder (2016) evaluated the carcinogenic potential of implanted synthetic mesh midurethral slings for SUI. They identified 2474 patients who underwent SUI surgery with a midurethral sling. With a medial follow up of 60 months, only 2 cancers (0.08%) developed following sling placement. Neither of these tumors had any relationship to the sling placement. Both tumors were of gynecologic origin (vaginal melanoma and ovarian tumor). There were no cases of sarcoma, bladder or urethral or squamous cell carcinoma identified. They concluded that with a medial follow up of 5 years after synthetic midurethral sling that the development of pelvic malignancy is rare (0.08%) and is unlikely to be related to foreign body reaction from the implanted material.

Adel (2016) reviewed the carcinogenic potential of polypropylene mid-urethral slings. The authors searched multiple online databases for information related to any possible carcinogenic potential of polypropylene mesh. They concluded that the likelihood the mesh causing malignancy is exceptionally low. To date, there is no reliable scientific data suggesting a link between Ethicon's polypropylene meshes and cancer.

Mesh Degradation

Plaintiff experts in the MDL cases allege that polypropylene mesh undergoes degradation. Over the last year, several studies have been published or presented that suggest that mesh does not degrade. For example, Ong (2016) presented an abstract at the International Urogynecological Association Meeting on the morphology and material chemistry of explanted Prolene meshes with a novel cleaning process that does not utilize formalin. With electron microscopy, they showed that the Prolene mesh did not undergo meaningful or harmful degradation in vivo. They found that there was a cracked layer over the Prolene fibers that was related to adsorption of the formalin fixative used in preparation of the explanted specimens.

Following up on their abstract, Thames (2016) was concerned with the cleaning protocol utilized to analyze mesh that has been removed from patients. They sought to create a nondestructive, hydrophilic cleaning process and utilize microscopy and spectroscopy of the specimens. 78 explanted Prolene meshes were analyzed that were implanted between 0.4 and 11.7 years. They concluded that their cleaning process of explanted Prolene meshes showed that they did not degrade in vivo. This confirms the

decades of excellent clinical results, in vivo stability, and biocompatibility of Prolene within the body. The authors further concluded that the cracked layer previously suggested to be degraded Prolene was actually due to adsorbed protein-formaldehyde coating from formalin fixation. This confirms similar findings of other authors who found no polymer degradation after cleaning the biofilm from the explants. (DeTayrac and Letouzey 2011).

D. Long Term Follow Up of Patients after TVT Procedures and Management of Complications, Sexual Function after TVT

Kuuva (2006) published their long term results (mean follow-up of 6 years) of the TVT operation in 129 women with SUI. The authors noted that no serious or unexpected adverse events were revealed. Specifically, they noted a cure rate of 81% via pad test at a mean time of 6 years since surgery. They noted a UTI rate in 9.3% of patients. The de novo urge rate was 4.7%, and the urge symptom cure rate was 88.9%. The authors reported tape visualization in 3.1% of patients, of which 1.6% had a resection due to subjective discomfort. As mentioned above, they authors noted that "no unexpected serious long-term complications were identified after the TVT procedure." They concluded that "the TVT operation appears to be a safe and effective anti-incontinence procedure in all female stress urinary incontinence subgroups." Additionally, the authors concluded by recommending "that the TVT procedure should be used as the primary operation for female stress urinary incontinence." Also in this 2006 study, the authors noted the TVT cure rates in various patient-types, including 80-91% cure at 4 year follow-up in primary cases; 80-88% in recurrent cases; and 80.5-

100% in groups containing both primary and recurrent cases. By contrast, the authors described studies showing the cure rate of the Burch colposuspension at 5 years or longer to range from 44 to 86%. Further, the authors described some of the complications with the Burch, including but not limited to: vault prolapse ranging from 7 to 8%, rectocele/enterocele rates ranging from 31 to 57%; cystocele rate of 25%; post-colposuspension (pain) syndrome following burch ranging from 2.3 to 12%, persistent voiding difficulties after Burch from 2 to 22% (necessitating urethrotomy in 3.7% of patients), de novo detrusor instability rate of 14.7%, and urge incontinence rate of 41%.

Svenningsen (2013) published their long term results (10.75 years) from the Norgwegian registry with Ethicon's retropubic TVT procedure. They analyzed 483 women with a median duration of follow up of 129 months. They noted an objective cure rate of almost 90% and a subjective cure rate of 76%. They noted subjective voiding difficulties in 22.8% of patients and de novo urge incontinence in 14.9% of patients at 10 year follow up. The authors acknowledged these results suggesting that the patients who were very satisfied with their procedure were almost identical among those with and without subjective voiding problems and no difference in low flow rates between groups. The authors went on to say that they consider it unlikely that the reported voiding difficulty represents a serious clinical problem for these women at present time. With regard to the reported rate of de novo urge incontinence of nearly 15% at 10 year follow up, the authors acknowledged that no questions explored the issue of de novo urgency without incontinence. All patients were unfortunately grouped into the above mentioned de novo urge incontinence group even if they did not have incontinence, which is a noted limitation of the study. The authors rationalize this by

saying that their rate of de novo urgency incontinence fits into the range of other publications, which has been reported to range from 1-17%. In identifying risk factors for failure after TVT, the authors concluded that "even though the long-term failure rates after retropubic TVT are low for the whole cohort studies, age ≥ 56 years, high degree of preoperative urgency incontinence symptoms, and surgical complications all exert a negative impact on the long-term outcome."

Additional TVT studies with 10+ year follow-up on the TVT include, but are not limited to: Nilsson 2008 (11 years); Olsson 2010 (11.5 years); Groutz 2011 (10 years); Aigmueller 2011 (10 years); Heinonen 2012 (10.5 years); Serati 2012 (10 years); Nilsson 2013 (17 years); Trabuco 2014 (10 years). Several large studies involving TVT with 5+ year follow-up includes: Ward 2008 (Ward-Hilton Trial); Kenton 2015 (TOMUS Trial); Celebi 2009; McCracken 2007; Liapis 2008; Prien-Larsen 2009; Song 2009; Angioli 2010; and Lee 2010. TVT-O has not been on the market as long as TVT, but some of the 5+ year studies on TVT-O include: Angioli 2010 (5 year); Groutz 2011 (5 year); Cheng 2012 (5 year); Serati 2013 (5 year); Athanasiou 2014 (7 year); Cheung 2014 (5 year); Laurikainen 2014 (5 year); Kenton 2015 (5 year); and Tommaselli 2015 (5 year). The long-term studies on TVT and TVT-O have consistently shown a favorable safety profile for both devices. This is also consistent with the safety information described in the level 1 literature and large patient registries. (Ford 2015 Cochrane Review; Schimpf 2014 SGS Systematic Review).

Pastore (2016) sought to evaluate the QOL and sexual function in women treated with TVT-O and single incision sling for SUI. In their evaluation of 42 patients, they noted a resolution of SUI in 90% of the single incision sling group and 86% of the

TVT-O group. Both groups had significant improvement in their scores on the Female Sexual Function Index (FSFI) scores. The authors concluded that both slings offered a high rate of continence and sharp improvement in all domains evaluated by the FSFI.

Brown (2016) published a review article on the evaluation and management of mid-urethral sling complications. The authors note that a mid-urethral sling is the standard of care for the treatment of female SUI. They sought to review the most recent literature regarding the intraoperative and post-operative management of mid-urethral sling complications. The authors note that the MUS is considered by many to be the standard of care for the treatment of SUI. They note comparable results for the Burch and autologous fascial slings. The authors describe common intraoperative complications and their management and advise that the best way to prevent complications with a MUS is to adhere to fundamental surgical procedures during the insertion. This information is well known to physicians and has been published in all major authoritative texts since the late 1990's. The authors then go on to describe the immediate post-operative complications and delayed post-operative complications.

Again, the authors stress that the clinical evaluation of such patients begins with a detailed clinical history and high index of suspicion as these complications can be subtle and difficult to identify. Again, this information is not new to physicians as authoritative textbooks have mentioned these complications for the last 20 years. The mentioned delayed complications of pain, dyspareunia, vaginal mesh exposure, bladder outlet obstruction, mesh perforation and urinary fistula are not new complications and have been described over 20 years ago, and with the exception of mesh exposure (which is essentially a wound complication), these are complications that are well known to

occur with any anti-incontinence surgery. The authors stated in their conclusion section that MUS should be performed by experienced surgeons as this may reduce the risk of complications. This is a logical suggestion, which echoes the manufacturer's IFU, which states that surgeons should be familiar with the surgical treatments of SUI and understand the indications and relevant anatomy before performing such procedures. The authors acknowledge that surgeons should have a high index of suspicion for mesh related complications and suggest that management can be challenging. While they state that complications may not always be reversible, they conclude that "nevertheless, despite the risk of complications, the MUS remains the standard of care for the surgical treatment of SUI for many practitioners."

Midurethral slings such as the TVT and TVT-O have known acceptable risks and have proven the test of time in becoming the worldwide gold standard treatment for stress urinary incontinence. As such, it is commonly known in the overwhelming majority of the pelvic floor surgical community, as evidenced by the vast body of medical literature, position statements, FDA statements, and guidelines, that the benefits of midurethral slings such as TVT and TVT-O substantially outweigh the risks and are reasonably safe for their intended use in treating stress urinary incontinence.

Synthetic slings are the most common type of surgical procedure performed today for SUI and monofilament, large pore polypropylene used in TVT is the most common type of synthetic material used in slings. Slings have a number of advantages over the Burch colposuspension procedure. In that procedure, the vaginal wall is attached to the Cooper's ligament adjacent to the public bone. A longer hospital stay is required. Surgical times and recovery times are longer. Patients often leave the hospital

with an indwelling urinary catheter. Wound complications and hernia can occur. While the laparoscopic Burch is considered to be less invasive than the open Burch, it is more difficult to learn and perform, must be performed under general anesthesia, requires multiple abdominal incisions, and has not shown to be superior to TVT or TVT-O in randomized controlled trials. Cadaveric slings, another surgical treatment option, are used less frequently for a number of reasons, including postoperative pain, voiding dysfunction, lack of durability and rejection issues.

As mentioned previously, the TVT was initially introduced in 1998 as a minimally invasive treatment for SUI. After more than six years of clinical success with TVT, Ethicon launched the TVT-O after years of research and studies performed by the inventor, Professor Jean de Leval, who introduced the inside-out transobturator approach, which differed slightly from Delorme's outside-in approach.

The Instructions for Use (IFU) that accompany the TVT-O device include warnings and precautions to physicians. The IFU emphasizes that physicians should be adequately trained in implanting TVT and should have sufficient knowledge of the pelvic anatomy to avoid large vessels, nerves, bladder and bowels. The IFU sets out potential risks and complications of the procedure, including the risks of punctures or lacerations of vessels, nerves, bladder or bowel. The IFU warns that a foreign body response may result in extrusion, erosion, fistula formation and inflammation. The IFU warns of the risk of infection and also warns against over-correction (too much tension of the tape). The IFU instructs surgeons on how to place the mesh tension free as follows, "Position the tape loosely e.g. without tension, and flat under the mid-urethra. At this stage a cough test can be performed. This allows adjustment of the tape so that only a few drops of

urine are lost during the cough…" The IFU goes on to warn that "Users [pelvic floor surgeons] should be familiar with surgical technique for urethral suspensions and should be adequately trained in the Gynecare TVT Obturator procedure before employing the Gynecare TVT Obturator device."

Further, the IFU mentions that the surgeon should be contacted immediately if dysuria, bleeding or other problems occur. Finally, the risk of de novo detrusor instability is discussed which can occur following sling procedures utilizing the Gynecare TVT-O system. Additionally, the TVT-O IFU warns of transient leg pain that usually be managed with mild analgesics. It is my opinion that the warnings in the TVT-O IFU provided surgeons with adequate and sufficient information about the product and the risks and potential complications at issue. It must be remembered that surgeons gain knowledge from multiple sources, including but not limited to the peer-reviewed medical literature and their clinical experience. My opinions regarding the adequacy of the TVT-O IFU are based on my clinical experience, my review of the medical literature, my experience teaching medical students, residents, and fellows on the IFU, my review of the FDA's labeling guidance, and discussions with colleagues.

Ethicon also prepared a brochure for patients. This patient brochure can never be a substitute for a meaningful conversation between the patient and her surgeon. This brochure mentions that difficulty urinating, pain with intercourse, scarring and exposure of the mesh can occur. It is the responsibility of any surgeon to ensure that the patient understands the potential risks and benefits of a procedure.

In addition, although it is the responsibility of any surgeon to ensure that he or she is properly trained to perform a procedure, the professional education provided by

Ethicon was comprehensive and well-designed. I personally attended formal presentations on the TVT Obturator and Prolift mesh at the Cleveland Clinic Foundation in 2005. This course was given on site at the Cleveland Clinic with their full-time faculty members. The course consisted of didactic lectures on prolapse and associated surgical procedures followed by a cadaver lab where faculty and preceptees worked hands-on to learn these techniques. Instructors told us that we could contact them after the course if we had any specific questions or problems.

In 2004, the TVT-obturator (TVT-O) procedure was introduced as a alternative and less invasive technique to treat SUI. The obturator based approach avoids the retropubic space and trocar passage is easier, as the risk of vascular, bowel and bladder injuries are greatly reduced. This is for several reasons including passage through the obturator space and modifications made to the trocar to make it more narrowed and curved to navigate the obturator foramen. When compared to the pubovaginal sling, the TVT and TVT-O procedures produce superior cure rates at short term follow up and lower rates of adverse events. Sartori and colleagues (2008) studied 80 patients with SUI. Among those, 61 underwent TVT and 19 a pubovaginal sling. After 6 months, 96.7% of women with TVT and 89.5% of those with a sling thought they were healed from the procedure. Urinary retention was observed in 42% of the pubovaginal sling cases and 9.8% of the TVTs.

All SUI procedures have risks and potential complications; these procedures can and do fail in some patients. All surgeries involve some pain or discomfort and a surgery is never a guarantee of a cure or a pain-free postoperative period. Risks of SUI surgery include anesthesia risks depending upon type, bleeding and transfusion,

hematoma, infection, wound complications, urethral injury, organ and nerve damage, voiding dysfunction, urinary retention, urinary frequency and urgency, pain (including pelvic pain), dyspareunia (pain during sexual intercourse), inflammation, scarring, adhesions, urinary tract infections, fistula, DVT and other major surgical risks and need for additional or repeated surgical procedures. These are risks that all urologists, ob/gyns and urogynecologists are trained about in residency and fellowship as well as thoroughly described in the medical literature in a variety of clinical settings, patient types, and levels of surgical experience. These risks do not need to be incorporated in the IFU because they must be considered and are known to any physician who performs pelvic floor surgical procedures. The TVT and TVT-O IFUs adequately and appropriately warn surgeons of the risks that are related to the clinical use of the device. While suture erosions and graft exposures can occur with Burch and autologous fascial sling procedures, respectively, mesh erosion and exposure are the only unique complications of synthetic midurethral slings (FDA 2013, AUA 2013).

Pelvic pain, dyspareunia and other pain are frequently found in women of various ages and in the general background populations. I commonly treat women with chronic pelvic pain and persistent dyspareunia who have never had previous surgical treatment for SUI or POP. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The chronic pelvic pain and de novo dyspareunia rates in patients who have received a TVT-O are extremely low. These complications are not new, and in fact, Francis 1961 published on dyspareunia with pelvic surgery, well before the age of pelvic mesh. The medical literature and my clinical experience demonstrate

that many women presenting with urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline.

Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction. Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth. Pelvic pain and other pain (inguinal and lower extremity related pain) is a known risk of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures. Of course, there are patients who have pelvic pain in addition to urinary incontinence and desire their incontinence treated. In the appropriate patient with urethral hypermobility and documented stress urinary incontinence, a TVT can be considered a first line treatment. Such patients may achieve a cure of their stress incontinence while their pelvic pain worsens. In my experience, this worsening of pelvic pain following TVT is unrelated to the TVT but rather is due to pelvic floor neural hypersensitivity. These patients with chronic pain and stress incontinence who desire a TVT (or another surgical treatment for incontinence) are warned about the possibility of worsening of pelvic pain after the anti-incontinence procedure.

Another potential complication of synthetic sling procedures is the risk of mesh exposure or erosion. This uncommon complication can usually be treated very easily. The FDA has noted the mesh exposure rate for synthetic midurethral slings to be

around 2%. (FDA 2013). This is consistent with larger reviews of the medical literature (Tommaselli 2015, Schimpf 2014, Novara 2008, Ford 2015, Unger 2014, Jonsson-Funk 2013, 2013, Nyguen 2012). Long-term studies evaluating the TVT-O have shown consistently low exposure rates over time, which suggests that most erosions or exposures occur within the first 12 months. Surgeon technique and volume also plays a significant role in the incidence of complications (Welk 2015). In this paper, the authors also discussed how most of the patients in their large population study who experienced a complication return to the implanting physician, which is contrary to a small tertiary study by Abbott (2014). In this latter paper, the authors noted that 50% of patients who sought treatment for a mesh complication at a tertiary care facility actually had their procedure performed at a different facility. The risk of erosion associated with sling procedures was well known among pelvic floor surgeons since their inception with the original TVT in 1998 and in fact before that as the medical literature reported on the use of synthetic materials to surgically treat SUI as well as potential complications including mesh exposure and erosion. In addition, all pelvic floor surgeons understand from their training and experience that no treatment is guaranteed to cure SUI and complications can always occur.

Plaintiffs' experts cite to Wang (2004) for the proposition that TVT is cytotoxic. Wang (2004) reported a 2.4% rate of defective vaginal healing and a 1 % incidence of persistent delayed healing of the anterior vagina, 1 to 7 years after the operation. They believe that vaginal erosion may occur after delayed infection of the synthetic sling or prominent foreign body reaction, which leads to separation of the vaginal incision and sling erosion. In their study, six women had complete epithelialization over the mesh

after 1 debridement of the vaginal tissue. They attribute these results to the presence of factors such as inadequate vaginal tissue coverage during the operation, rigidity of the mesh and its propensity for injury to adjacent tissues, or a site-specific, localized inflammatory response of the suburethral vagina is also plausible. Moreover, in patients with complete epithelialization of the mesh who later had removal for other reasons, several patients displayed evidence of foreign body reaction, dense fibrosis, and occasional perivascular mononuclear cell infiltration. Thus, the inflammatory histologic reaction associated with slings can be present in slings that have extruded, have epithelialized, or appear completely normal upon examination. This is especially true considering that cell death is naturally occurring without any association of mesh. As such, this study does not support the theory that mesh exposures are caused by an alleged cytotoxic reaction. Similar studies (Hill 2015; Klosterhalfen 2002) evaluating inflammatory responses found that there was no association between pelvic pain and a chronic inflammatory response.

Plaintiffs' experts rely on one study to support their theory that a partially absorbable mesh would be a safer alternative to TVT mesh. Okulu (2013), a study from Turkey, evaluated complication rates of mixed types of mesh materials over a 4 year period in 144 women with SUI. They utilized Vypro (semi-absorbable multifilament plus absorbable polyglactin), Ultrapro (semi-absorbable monofilament + nonabsorbable polypropylene) and compared that to Prolene light mesh. All three groups exhibited similar continence rates at four years follow up. Interestingly, vaginal erosions of mesh were noted in all groups, which by plaintiffs' experts' logic would suggest that these meshes are also defective. Plaintiffs' experts also fail to apply the same criticisms

of their criteria for a long-term study by readily accepting the results of this four-year study using hand-cut slings to support their safer alternative design theory. The sample size of this study is insufficient to compare these exposure rates to TVT mesh. De novo urgency and incontinence were also observed in all groups. The procedures performed in the Okulu study differ from midurethral sling procedures.[1] Ironically, plaintiffs' experts wrap up the basis of their opinions in this one study, in which the authors have specifically identified a comparative weakness of their study, concluding that, "This surgical method also needs evaluation, especially in comparison with the traditional TVT sling procedure." Further, plaintiffs' experts have failed to test or replicate the results of the Okulu study in their own patients.

In 2010, Ethicon considered Ultrapro as a novel concept for slings but the sterilization process made the Ultrapro stick to the side of the sheath and caused the mesh to stretch out (Elbert R&D Memorandum 12.2.2012). Further, in a SCION PA/SUI Treatment Unmet Needs Research Panel 1.22.2010, roughly 65% of physicians believed that partially absorbable mesh would not have any potential benefits. Further, they would want to see at least 2 years of clearly beneficial efficacy data before considering this potential treatment. Many are concerned that the use of a partially absorbable mesh is

[1] "This patch was 3 - 4 cm in most of the patients. The size of the mesh was individualized during the procedure. The proximal anterior vaginal wall (the lower part of the "A") was dissected as a flap (Figure 2a). Synthetic mesh materials were first sutured onto the upper part of the A on the vaginal island with absorbable Vicryl_ sutures. Then, with two polypropylene sutures, these meshes were fixed on both the right and left sides of the island in a helical manner to form a suspension, and using curved Kishner needles, the prolene sutures were transferred to the suprapubic area. Thus, the meshes were fixed with two polypropylene sutures, and the sutures moved to the suprapubic area using Kishner needles at the same point where they were tied down. These sutures were ligated on the fascia of the rectus muscle in a crosswise manner (Figure 2b). The mobile lower wing was advanced onto the island and sutured onto the vaginal skin with intermittent sutures using 3-0 Monocryl sutures (Figure 2c). Cystourethroscopy was performed to achieve control of the bladder and urethra after passage of the needle. After confirmation that the bladder and urethra were normal, the Prolene sutures were ligated crosswise in the suprapubic region. Special attention was paid not to create much tension on the mesh material."

like the worst of two worlds. The sling will be weaker because of absorption and there is still the presence of synthetic material in the body. Finally, in a letter from the FDA to Ethicon on December 21, 2010, this device was rejected by the FDA because if lack of superiority to current available products (TOPA TVTO-PA 510K Rejection Letter). The suggestion that a lighterweight, larger pore, partially absorbable, laser cut mesh is safer than mechanically cut TVT and TVT-O has not been verified in any reliable clinical studies, and therefore lacks any scientific basis for such an opinion.

Multiple studies and professional society consensus statements, surveys, and clinical practice guidelines, including but not limited to AUGS, SUFU, AUA, IUGA, NICE, EAU, and ACOG, have confirmed that midurethral synthetic slings are the treatment of choice and the standard of care for the surgical treatment of SUI. The 2014 (revised in 2016) AUGS and SUFU position statements highlight three important facts about synthetic mid urethral slings. (1) Polypropylene material is safe and effective as a surgical implant. (2) The monofilament polypropylene mesh MUS is the most extensively studied anti- incontinence procedure in history. (3) Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients. Similarly, the AUA released a position statement approved by the Board of Directors in 2011 and revised in 2013, stating in part, "Extensive data exist to support the use of polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of

these complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well." Other organizations and societies, including the AUA, IUGA, ICS, NICE, EAU, and others have come to similar conclusions regarding the safe, efficacious, and primary use of synthetic polypropylene midurethral slings.

E. Pertinent Outcome Data available to all physicians who perform TVT and TVT-O procedures. Considerations for discussions with patients in the pre- and post-operative period.

Since the introduction of the TVT in 1998 and TVT-O in 2004, there have been hundreds of RCTs and thousands of other papers reporting the safety and efficacy of these procedures which utilize the same Prolene mesh, including numerous long-term studies. These papers have also been presented in regional, national and international meetings as well as CME conferences both live and on-line, and are often delivered to doctors' offices from various journal subscriptions. Similarly, papers have been presented and published regarding the challenges with the procedure, follow up and patient selection. It is the responsibility of each implanting physician to be up to date regarding new data pertinent to their practice. Of particular importance is the relevance of preoperative voiding symptoms, the role of multiple pelvic surgeries performed at the same time in addition to sling and sexual pain unrelated to the mesh itself.

Regarding the relevance of preoperative voiding symptoms, patients who only have stress incontinence do best when a sling is performed. However, patients with mixed UI tend to do worse. Aigmueller (2011) reported a 10 year follow up of patients after TVT procedure studying 117 patients. Subjectively, 6.4% considered themselves to

be unchanged and 11% considered themselves to be worse in terms of their leakage after sling. They reported that 37% of patients with preoperative mixed urinary incontinence still had urge urinary incontinence post operatively. Their reported rate of detrusor instability was 20%. This data was similarly reproduced by Svenningsen and associates (2012) who reported that 23% of patients had subjective voiding difficulties and denovo urinary incontinence increased from 4.1% after surgery to 15% at 10 year follow up. Groutz in 2011 reported that patients who had surgical treatment failure after sling procedures are more likely to have recurrent UTI and post operative incomplete bladder emptying. In another paper by Groutz (2011), preoperative detrusor overactivity was reported as an independent risk factor for sling failure. Aigenmueller (2014) looked specifically at reasons for dissatisfaction with sling procedures. They noted that 15% of patients were worse after their sling. This was most prevalent in patients with preoperative urge urinary incontinence. The authors go on to suggest that patients should be counselled that if they have mixed urinary incontinence and recurrent UTI preoperatively that they are at higher risk for failure of their sling and dissatisfaction in the results of their surgical procedure. The abovementioned papers are significant and these results mentioned to at risk patients prior to and after performing sling procedures at each office visit with the patient.

The risk of performing multiple surgical procedures at the same time must also be considered by the operating surgeon. If a surgeon is considering a hysterectomy, prolapse repair and sling, the risk of all of these procedures should considered as potentially additive and a detailed discussion with the patient must be undertaken. Abdelmonem (2010) evaluated the vaginal length and dyspareunia after TAH and TVH.

Postoperatively, there is a significant decrease in vaginal length by approximately 2 cm in the TVH group. This is statistically significant when compared to no loss of length in the TAH group. There is a significant increase in dyspareunia in the TVH group as compared to the TAH group. The authors theorize that this decrease in length is due to redundant trimming of the vaginal wall during vaginal prolapse repair. Further, Athanasiou (2014) reported on the 7 year follow up of outcomes of TVT-O. The authors found that when multiple procedures are combined that the subjective cure rate for incontinence was lowest. Specifically, when TVT-O is performed as the sole procedure, 90% of patients have an objective cure rate. However, when hysterectomy is combined with pelvic floor reconstruction and TVT-O sling procedure, the objective cure rate decreases to 74%.

Finally, it is known to all surgeons who perform pelvic floor surgery that there are significant risks of sexual dysfunction post operatively. While the literature and patient brochure mentions that sexual intercourse pain can result, there are inherent risks of pelvic surgery that must mentioned to all patients. Tucker (2015) reported in 119 patients who underwent risk reducing salpingo-oopherectomy. Of these 119 patients, 72% underwent concomitant hysterectomy. They found that 74% of patients had postoperative sexual dysfunction including 44% with lubricating difficulty, 41% with reduced sexual satisfaction, 28% with dyspareunia and 28% with orgasm difficulty. Thus, the risks of not only dyspareunia but the entire spectrum of female sexual dysfunction must be discussed with all patients who undergo any type of pelvic floor surgical procedure.

F. Physician Education about Incontinence Surgeries at the Time of TVT's Release

Physicians learn about how to perform incontinence surgeries from their education and residency training. They can also learn these techniques through fellowships, mini-fellowships, preceptorships, and proctorships. However, the core backbone of learning is from the readings in core textbooks. In this section, I will describe the contents of core textbooks that were available to physicians in the 1995–2000 time period, around the time of the launch of TVT in 1998.

Physicians who perform incontinence surgery come from one of three specialties and each will be addressed separately: (1) urology, (2) obstetrics and gynecology, and (3) urogynecology (now known as Female Pelvic Medicine and Reconstructive Surgery). One core textbook from each specialty is discussed below, although several other textbooks were available at the time of TVT's launch.

Urology

Campbell's Urology (7th Edition, 1998; Walsh, Retik, Vaughan and Wein) was and remains one of the core urology texts for urology residents and practicing physicians. Practitioners will refer to this text beyond their residency and into practice to learn about core topics and surgical procedures. The 7th Edition of Campbells was published in 1998, around the initial launch of TVT. Accordingly, if a physician were interested in a synthetic sling procedure for incontinence, this would have been the textbook they would refer to.

Chapter 32, "Vaginal Reconstructive Surgery for Incontinence and Prolapse," provides a great deal of information for the clinician. First, the chapter describes that

surgery for SUI is indicated in motivated patients with significant loss of urine, creating a social or hygienic problem.[2] Thus, these procedures are not for everyone and the type and severity of SUI, degree of associated pelvic organ prolapse must be considered. Further, a successful outcome should be based on the ability of the treatment to have a positive impact on the patient's quality of life.

Next, a description of each of the surgical procedures is undertaken. Chapter 32 describes several different surgical options:

- Stamey Bladder Neck Suspension: This procedure uses a knitted synthetic Dacron graft to support the bladder neck. The authors stress the need for a cystoscopy during this procedure to exclude bladder injury. The authors specifically warn of the risks of erosion of suture or bolster material into the urinary tract, infection, postoperative pain, and urinary retention.[3]
- Raz Bladder Neck Suspension & Gittes Bladder Neck Suspension: These two procedures use polypropylene sutures to support the bladder neck. The authors again note the importance of cystoscopy to check for bladder injury. For the Raz suspension, the authors note several short-term complications (including vaginal spotting, urinary tract infections, and irritative symptoms) and long-term complications (including de novo urge incontinence, enterocele, prolonged voiding dysfunction and suprapubic pain). The book also discusses potential complications for the Gittes procedure, including urinary retention,

[2] *Campbell's Urology* (7th ed.), at 1066.
[3] *Id.* at 1068.

suprapubic pain or cellulitis, vaginitis, suture infection (with abscess formation), and genitofemoral nerve entrapment. [4]

- Raz Vaginal Sling: This procedure uses a #1 Prolene suture to support the bladder neck and urethra. Again, the authors stress the use of cystoscopy to ensure that no bladder injury has occurred. The authors discuss the need to ensure that sutures are not placed under tension, similar to the tension-free placement of the TVT procedure. Complications for the Raz vaginal sling discussed in the book include recurrent incontinence, enterocele, prolonged urinary retention, and suprapubic pain.[5]

A lengthy section within Chapter 32 discusses the potential complications of vaginal surgery. The section highlights that the vast majority of complications are preventable when the surgeon is aware of the hazards and risk factors in any given patient based on her postoperative history, physical examination, and preoperative tests. It further mentions that early recognition and appropriate intervention can minimize any sequelae.[6] Several of these complications are discussed in great detail:

- Bleeding: Pelvic hematomas can result from dissection in the wrong fascial planes as well as with dissection into the retropubic space. Methods to deal with such bleeding are discussed including packing, electrocautery and

[4] *Id.* at 1070–71.
[5] *Id.* at 1074.
[6] *Id.* at 1089.

balloon tamponade. Embolization for severe bleeding is discussed as well as laparotomy.[7]

- Neurologic Injury: This complication can range from transient neurapraxia to severe axonotmesis, which can take months to recover. These injuries can result from positioning but also through dissection into the retropubic space. Discussion of the potential of gentofemoral, femoral, saphenous, sciatic, pudendal and obturator nerves are discussed. These injuries can be due to a number of causes including patient positioning, dissection and placement of needles during suspension procedures.
- Bladder Injury: This complication can result from misplaced or deep operative incisions over the anterior vaginal wall, misplaced sutures, perforation during suture transfer, excessive electrocautery, or extreme medial displacement of the scissors when entering the retropubic space. The book discussed the importance of intraoperative cystoscopy as well as strategies for how to deal with such an injury. Further, the discussion of delayed recognition of suture material is mentioned. The importance of recognizing that postoperative irritative voiding symptoms as persistent UTI must be recognized. If the sutures are found, these can be removed with endoscopic scissors.[8]
- Ureteral Injury: Injury to the ureters is reported to occur during vaginal surgery in up to 1.5% of cases. The chapter discusses risk factors for ureteral injury that all physicians should know about, including a history of endometriosis, prior pelvic or vaginal surgery, and the presence of pelvic

[7] *Id.* at 1090.
[8] *Id.* at 1091.

organ prolapse including entities such as enterocele, large cystocele, or uterine procidentia. The text is clear that the diagnosis of ureteral injuries requires a high index of suspicion and should be confirmed with cystoscopy with retrograde pyelography or urogram.[9]

- Infection: The infection of sutures and other permanent graft materials can result from vaginal contamination and should occur in less than 1% of patients. Pain is a common complaint. Lower urinary tract infections are common in the first month after vaginal surgery and often respond to a short course of antibiotics. However, persistent UTI may be the presenting complaint when erosion of suture and bolster materials occurs in the urinary tract. This can cause delayed symptoms occurring months to years later.[10]
- Pain: Postoperative pain is discussed in detail in this chapter. Postoperative pain may be related to suspension sutures and generally subsides within a few weeks. Persistent pain is often idiopathic in nature but can be caused by entities such as cellulitis, nerve entrapment (ilioinguinal nerve), muscle entrapment, and vigorous overtying of sutures. The chapter goes on to say that removal of sutures should be considered for patients with chronic pain.[11]
- Vaginal Stenosis (Shortening): Vaginal stenosis or shortening is described in this chapter in detail. This may result from excessive plication of the vaginal epithelium during closure or secondary scarring following hematoma formation in the vaginal vault. The chapter warns physicians to consider this

[9] *Id.*
[10] *Id.*
[11] *Id.*

possibility in patients with new onset dyspareunia, pelvic pain or vaginal pain.[12]

- Bladder Dysfunction: Temporary voiding dysfunction is common after pelvic reconstructive surgery and changes in voiding patterns, including obstructive voiding symptoms and mild bladder irritability should be explained to patients preoperatively. The chapter reports that transient urinary retention may occur in up to 40% of patients, but the incidence of prolonged retention is still significant at approximately 5%. Temporary need for self-catheterization may be possible, but urinary retention lasting longer than six months is rare. If this is the case, the text suggests that urethral obstruction may be occurring. This may be intraluminal from misplaced graft material or sutures. However, this obstruction can also be extraluminal from scarring or a retroperitoneal hematoma. The text mentions different treatment options including CIC, cutting or removing permanent suture material, and transvaginal urethrolysis.[13]
- Persistent Incontinence: Continued postoperative incontinence can be due to malposition of the suture or sling. If this is the case, the text suggests proper suture or sling placement may correct the problem. If the problem is due to unrecognized intrinsic sphincter deficiency ("ISD"), that may need to be treated with other modalities.[14]

[12] *Id.* at 1092.
[13] *Id.*
[14] *Id.*

These complications are all possible, to varying degrees, with any pelvic floor surgery, including TVT. A breakdown of complications in the AUA 2012 Updated Guidelines Appendix demonstrates the lower rate of complications from synthetic midurethral slings compared to the Burch Colposuspension and autologous fascial sling procedures.

Chapter 33, "Retropubic Suspension for Female Sphincteric Incontinence," describes retropubic urethropexy, an additional approach for pelvic floor surgery. There are two major retropubic urethropexy procedures: the Marchall-Marchetti-Krantz procedure and the Burch operations. These procedures are discussed in detail including the complications. Complications include those common to any surgical procedure, for example, infection and bleeding, injury to the urethra, bladder, or ureter can also occur during the procedure, and the patient must be evaluated for these problems intraoperatively.[15]

Chapter 34, "Pubovaginal Slings," discusses the indications and risks of pubovaginal sling surgeries using a variety of sling materials. Both autologous and synthetic materials (including polypropylene and mersiline) are described. The chapter references these synthetic materials described as early as 1961 by Williams and Te Linde. The chapter mentions the complications associated with synthetic slings, including significant morbidity, suprapubic abscess, sling erosion into the bladder, and delayed transection of the urethra. Further, the authors note that polypropylene slings have been associated with complications including urethral sloughing.[16]

Discussion of the preoperative evaluation, informed consent issues and complications are discussed in detail. If postoperative incontinence occurs, the authors

[15] *Id.* at 1091–1101.
[16] *Id.* at 1105.

recommend a urodynamic study to evaluate the problem. Persistent or de novo detrusor instability can result after sling procedures. The authors recommend surgeons to warn patients that return of normal voiding function may be delayed and that clean intermittent catheterization (CIC) may be required until normal function returns. They note that factors that may impair the return of voiding function include high sling tension, poor detrusor function, additional surgery such as cystocele or rectocele repair, and temporary overdistension from too long an interval between intermittent catheterizations. Long-standing inability to void is an unusual problem which may require additional evaluation and treatment. Physicians are advised to recognize bladder injury with careful placement of trocar needles and cystoscopy with a 70 degree lens. Sling tension adjustment is also performed such that the sling lies flat and is symmetric.[17]

Obstetrics and Gynecology

Danforth's Obstetrics and Gynecology, 7th Edition (1994), authored by Scott et al., will be discussed. In Chapter 46, "Urogynecology," the surgical treatment of stress incontinence is reviewed. Selection of a surgical procedure for a given patient has, until recently, been based on the operating surgeon's impression of the clinical complaints in the physical examination findings. Thus, multiple approaches can be considered for pelvic floor surgery.

The Chapter discusses retropubic urethropexy. There are two major retropubic urethropexy procedures: MMK and Burch. These procedures are discussed in detail including the complications. The chapter is specific to mention that complications include

[17] *Id.* at 1105–06.

those common to any surgical procedure, especially infection and bleeding can occur. Urethral, ureteral, and vesical injury may occur during the procedure, and the patient must be evaluated for these problems before leaving the operating room. This is a critical statement that complications must be anticipated, evaluated promptly, and addressed effectively as soon as possible. A major complication is obstructive voiding postoperatively, and if that is persistent, it can be managed by intermittent self-catheterization. A long-term complication is the development of an enterocele. This chapter discusses success rates for the retropubic urethropexy which range from 80% to 90% after one year in studies reporting objective preoperative and postoperative urodynamic data.[18]

Combined retropubic and vaginal approaches are also described. The combined vaginal-retropubic approach was first popularized by Pereyra in 1956. The chapter is quick to point out, that the entire group of vaginal retropubic approaches to the treatment of stress incontinence did not enjoy the same success rate as procedures performed primarily through the retropubic space, because the suture material itself is relied on to provide permanence for the operation. The chapter describes the surgical technique for the modified Pereyra procedure which uses an anterior vaginal wall incision in a manner similar to that used for the traditional anterior vaginal repair. Permanent sutures such as Prolene, Gore-Tex, and 0-nylon are used in this procedure. The chapter again points out to the surgeon to confirm that no sutures are located inside the bladder. Cystoscopy is used for this purpose. While it is highly unlikely that sutures will be found in the bladder, this is an important step for identifying any intra-operative complications

[18] *Danforth's Obstetrics and Gynecology* (7th ed.) at 860.

or perforations. Complications of this procedure are well described in this Chapter. These complications include possible injury to the bladder, urethra, and ureters, and possible injury must be determined at the time of the surgical procedure. Infection and hemorrhage can also occur. The complications discussed previously for obstructed voiding postoperatively are identical.[19]

This Chapter also discusses the suburethral sling procedures. Of note, this Chapter was written in 1994, three years prior to the release of the TVT. The concepts in this Chapter are applicable to physicians using the TVT. The Chapter describes that suburethral sling procedures were first described in the early 1900s by Giordano. Sling procedures are used in primary and secondary cases for support of the urethrovesical junction. Suburethral sling procedures may use autologous materials or foreign materials to provide support. Autologous materials such as fascia lata may be obtained from the leg, and rectus fascia from the rectus muscle has also been used. The chapter also mentions synthetic materials such as Marlex, Mersilene, and Vicryl meshes as well as Gore-Tex patches had been used for suburethral sling with success. As this Chapter demonstrates, information about using synthetic slings was actually already known by physicians well before TVT's entrance into the marketplace. A detailed discussion of the sling procedure is provided. Complications of this procedure are well-described. Ten percent of patients may need to do intermittent self-catheterization. Most patients accept this, because it is preferable to having continued urine loss. The Chapter discusses complications of this procedure including the possibility of erosion of the sling material into the vagina or the anterior abdominal wall with sinus tract formation.

[19] *Id.* at 861.

The Chapter notes that slings must be removed because of this problem. The Chapter goes on to state that slings may also be removed from patients who developed marked obstruction and did not want to use self-catheterization on a permanent basis. This is the reason why urethrolysis is an important procedure it should be a part of the armamentarium of all pelvic floor surgeons. The Chapter makes it clear that elevation of the ureterovesical junction usually is permanent, and recurrent incontinence does not result after a sling is removed. Thus, in patients who need to have a urethrolysis, most patients will not require an additional incontinence procedure.[20]

Urogynecology (Pelvic Floor Reconstructive Surgery)

Chapter 14 of *Urogynecology and Pelvic Floor Reconstructive Surgery*, 2nd Edition (Walters and Karram, 1999), describes retropubic operations for stress incontinence. The Burch colposuspension and MMK procedures are discussed. Paravaginal defect repair is also described. Complications of pelvic floor surgery are described in detail. Short-term complications include wound infections and urinary tract infections. Direct surgical injury to the urinary tract can also occur, but rarely. Bladder lacerations occurred in less than 1% of patients. Sutures to the bladder and urethra and catheters sewn into the urethra occurred in less than 1% of patients. Ureteral obstruction occurred rarely. Accidental placement of sutures into the bladder during colposuspension or paravaginal repair, resulting in bladder stone formation, painful voiding, recurrent cystitis, or fistula, can occur but is rare. Ureteral obstruction occurs rarely after Burch colposuspension and results from ureteral stretching or kinking after elevation of the

[20] *Id.* at 863.

vagina and bladder base. Lower urinary tract fistulas are uncommon after retropubic procedures, with serious types occurring after less than 1% of the MMK procedures.[21]

Next, postoperative voiding difficulties are discussed. The incidence of voiding difficulties after colposuspension are reviewed. Urinary retention lasting greater than 30 days is rare. The Chapter notes that colposuspension procedures can change the original voiding pattern and introduce an element of obstruction that could disturb the balance between voiding forces and outflow resistance, resulting in immediate postoperative as well as late voiding difficulties. As such, pelvic floor surgeons are expected to be aware of this as any pelvic floor surgery can result in postoperative voiding dysfunction.[22]

Detrusor instability is also described. Detrusor instability is a recognized postoperative complication of retropubic procedures. Unstable bladders as demonstrated on cystometrogram have been reported in approximately 25% of patients with SUI and stable bladders preoperatively, with follow up to five years after Burch colposuspension. The mechanism of detrusor instability is not well understood according to the texts; this may be caused by disruption of the autonomic innervation of the bladder, although this relationship has not been proven.[23]

The authors also discuss osteitis pubis, which is a painful inflammation of periosteum, bone, cartilage, and ligaments of structures of the anterior pelvic girdle. It is a recognized postoperative complication of urologic and radical gynecologic procedures

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[21] *Urogynecology and Pelvic Floor Reconstructive Surgery,* 2nd Edition (Walters and Karram, 1999) at 166.
[22] *Id.*
[23] *Id.* at 167.

involving the urinary bladder. Physicians performing pelvic floor surgery recognize that enteroceles and rectoceles can occur after pelvic floor reconstructive surgery.[24]

Chapter 15 discusses surgery for SUI. A discussion of anterior repair with suburethral plication is first discussed. Next, a discussion of transvaginal needle suspension procedures is undertaken. This includes a modified Pereyra procedure as well as the Stamey procedure. The Raz procedure is also discussed. The text is clear to point out that cystoscopy is performed to assess for bladder injury or stitch penetration. This chapter also has a table that compares differences among the different suspension procedures, and demonstrates the importance of cystoscopy for any pelvic floor procedure. Cystoscopy is performed to either rule out injury, or confirm appropriate suture placement.[25] These comments on the use of cystoscopy can certainly be applied to the TVT procedure.

Next, a detailed discussion of suburethral sling procedures is undertaken. The Chapter mentions that the first-line operation was performed in the early 1900s using a gracilis muscle flap. Different modifications were undertaken over time. The chapter is clear to point out that this operation should be used with caution in patients with incomplete bladder emptying secondary to detrusor dysfunction. Further, the Chapter discusses that all patients undergoing sling procedures should be taught intermittent self-catheterization preoperatively. A history of pelvic radiation and the presence of a urinary fistula should also be considered relative contraindications because they may predispose the operative site to tissue breakdown, especially if synthetic material is used.[26]

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[24] *Id.* at _167.__.
[25] *Id.* at 175.
[26] *Id.* at 179.

The Chapter provides a discussion about the TVT as an ambulatory procedure for the treatment of stress incontinence. The Chapter mentions the importance of cystoscopy during the procedure to make sure there is no bladder or urethral injury. The Chapter discusses the importance of how the plastic sheath is removed, and that the sling material is not fixed to the endopelvic fascia or rectus fascia, but is simply cut on each side at the level of the skin.[27]

Next, a detailed discussion of complications of vaginal procedures for stress incontinence is discussed. First, a discussion of lower urinary tract injury is undertaken. The Chapter states that injury to the bladder or urethra can result from any of the vaginal procedures described for stress incontinence. Injury to the bladder and urethra should be repaired in layers at the time of the injury and continuous bladder drainage be continued for up to 14 days to allow adequate healing. The Chapter states that intraoperative cystoscopy is mandatory and should identify bladder injury or inadvertent stitch penetration. If intravesical suture is noted, it should be removed and passed again under direct finger guidance. Unrecognized injury or suture penetration in the bladder can result in postoperative voiding dysfunction, postoperative UTI, or formation of bladder calculi. Injury to the ureter during the vaginal operations for stress incontinence is rare, but possible. These statements are also applicable to the physician would perform a TVT because these are the same complications that they could encounter.[28]

Next, a discussion of postoperative voiding dysfunction and retention is undertaken. Voiding dysfunction and retention can occur after incontinence surgeries. The Chapter describes the reasons for retention, which may include advanced anterior

[27] *Id.* at 182.
[28] *Id.* at 184.

vaginal wall prolapse and the extensive dissection needed to repair it. The authors also believe that these procedures are associated with a higher incidence of postoperative voiding dysfunction and irritative bladder symptoms. Suburethral sling procedures can cause an increase in urethral outlet resistance. Most complications related to these procedures are secondary to obstruction and result in various forms of voiding difficulty and even permanent urinary retention. The Chapter also discusses the need to consider surgical intervention to take down the repair or loosen the sling in instances of severe voiding dysfunction or retention. It is these lessons that physicians will apply to these new situations (referring to TVT).[29]

Next, a discussion of detrusor instability and irritative bladder symptoms are discussed. The Chapter mentions that postoperative detrusor instability with urinary urgency, frequency, or urge incontinence can occur in up to 50% of patients after various operations for stress incontinence. This may be because of pre-existing detrusor instability, now unmasked, with increased bladder volumes caused by a return of outflow resistance, or new onset instability possibly related to infection, foreign body reaction, denervation, or anatomic urethral obstruction. This Chapter notes that up to 50% of patients who have undergone a suburethral sling will develop irritative bladder symptoms such as urinary urgency, frequency, nocturia and dysuria. These are subjective complaints that are not often documented on postoperative urodynamics.[30]

Recurrent or persistent incontinence is also discussed. The most common cause of recurrent incontinence after needle suspension is worsening of genuine stress incontinence because of failure to adequately support the urethra or there is ISD. The

[29] *Id.* at 184.
[30] *Id.*

chapter notes that it is difficult to determine whether postoperative instability developed de novo or was present preoperatively and either persisted or worsened.[31]

Next, a discussion of bleeding complications is mentioned. This is because all of the vaginal operations for incontinence described in this Chapter can result in bleeding. Excessive bleeding and hematoma formation are more common in procedures that require vaginal entry into the retropubic space.[32]

A detailed discussion of infection and erosion is described. A subset of complications including erosion, infection, and sinus formation occur more commonly when synthetic materials are used for sling placement or buttresses are placed during needle suspension operations. The Chapter notes that a small proportion of patients may require removal of an eroded permanent suture. These problems sometimes are exacerbated further by coexisting infection. The Chapter mentions that a few cases can be managed conservatively, but the majority of the patients will require removal of the foreign body or the sling material.[33]

A detailed discussion of nerve damage is also undertaken. Nerve damage can result from positioning in the dorsal lithotomy position. The nerve most commonly involved in this situation is the common peroneal nerve, but injury to the obturator, sciatic, tibia, fibula, or saphenous nerves can also occur. The Chapter points out that surgical injury to the ilioinguinal nerve can occur during the placement and tying of sling material or suspension sutures during transvaginal needle procedures. These patients will present with complaints of pain in the medial groin and inner thigh.

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[31] *Id.* at 185.
[32] *Id.*
[33] *Id.*

G. Additional Literature

In addition to these core textbooks, other medical literature available before or shortly after the release of TVT reported on the potential complications associated with surgical treatment of SUI. Reported complications included dyspareunia, pelvic pain, erosion, infection, de novo urge incontinence, and recurrent SUI. These were well known complications with any incontinence surgery.

Iglesia and others (1997), surveying the peer-reviewed literature, reported on several potential complications related to suburethral slings using synthetic mesh, including polypropylene mesh. Reported complications included dyspareunia, groin or suprapubic pain, erosion, graft infection, voiding dysfunction, urinary retention, rejection of the implant, recurrence, vesicovaginal fistula, and need for revision or removal of the implant. The authors also noted similar complications related to synthetic suburethral slings made of other synthetic materials.[34]

Chaikin et al. (1998) reported on 251 consecutive patients who underwent a pubovaginal fascial sling procedure before 1998. Reported complications included de novo or persistent urge incontinence, permanent urinary retention, bladder injury, prolonged pain, and SUI recurrence. [35]

Czaplicki and others (1998) reported on 81 patients who had undergone an MMK procedure between 1980 and 1994. The authors noted that cure rates decreased over time, with a 5-year cure rate of 57% and a 10-year cure rate of 28%. The authors

[34] Iglesia, et al. (1997).
[35] Chain, et al. (1998).

reported that 11% of patients experienced dyspareunia. Other reported complications included urinary infection, wound infection, nocturia, and recurrent incontinence.[36]

The authors in Chaliha et al. (1999) performed a comprehensive review of studies published between 1966 and 1997 related to complications associated with surgical treatment of SUI. This review covered several major surgical options used at the time, such as Burch, bladder neck suspensions, MMK, and sling procedures. Reported immediate and short-term complications included hemorrhage, urinary tract or visceral injury, urinary tract infection, wound infection, fistula, nerve injuries, and voiding dysfunction. Reported long-term complications (more than 6 weeks) included dyspareunia, groin pain, detrusor instability, and genital prolapse.[37]

In Demirci et al. (2001), the authors discuss a 220-patient study of women who had undergone a Burch procedure between 1994 and 1999. The authors noted a decreasing cure rate over time, with a 3-year cure rate of almost 84%, but a 6-year cure rate of 68%. Reported complications included pelvic organ prolapse, dyspareunia, groin or suprapubic pain, and voiding difficulty. The authors noted that reported rates of long-term dyspareunia associated with Burch ranges from 2% to 4%, with reported rates of groin or suprapubic pain as high as 12%. The authors also noted that the Burch may aggravate posterior vaginal wall weakness, leading to enterocele, as reported in prior literature.[38]

These publications and core textbooks demonstrate that, at the time of TVT's initial release, the medical community was well-aware of the potential risks and

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[36] Czaplicki, et al. (1998).
[37] Chaliha, et al. (1999).
[38] Demirci, et al. (2001); *see also* Galloway et al. (1990); Wang (1996).

complications associated with all pelvic floor surgeries, including SUI treatments using various native tissue, graft, and synthetic mesh materials.

H. Discussion of Synthetic Slings, Literature Review and Complications

Synthetic slings are the most common type of surgical procedure performed today for SUI and monofilament, large-pore polypropylene used in TVT is the most common type of synthetic material used in slings.

Slings have a number of advantages over the Burch colposuspension procedure. In that procedure, the vaginal wall is attached to the Cooper's ligament adjacent to the public bone. A longer hospital stay is required. Surgical times and recovery times are longer. Wound complications and hernia can occur. The laparoscopic Burch is less invasive but is more difficult to learn and perform, must be performed under general anesthesia, and requires multiple abdominal incisions. Cadaveric slings, another surgical treatment option, are rarely used for a number of reasons, including lack of durability and rejection issues.

When compared to the pubovaginal sling, the TVT procedure offers superior cure rates at short term follow up and lower rates of adverse events. Sartori and colleagues (2008) studied 80 patients with SUI. Among those, 61 underwent TVT and 19 a pubovaginal sling. After six months, 96.7% of women with TVT and 89.5% of those with a sling thought they were healed from the procedure. Urinary retention was observed in 42% of the pubovaginal sling cases and only 9.8% of the TVTs.

Pelvic pain, dyspareunia, and other pain are frequently found in women of various ages and in the general background populations. As previously discussed,

dyspareunia following vaginal surgeries has been described beginning in 1961 by Francis in a review of 385 women who underwent vaginal operations for a variety of conditions. The most common cause of dyspareunia in these patients related to narrowing of the introitus and vagina from removal of vaginal tissue as part of the treatment for their condition (prolapse). Thus, dyspareunia after vaginal surgery certainly existed many years prior to the introduction of biologic and non-biologic materials to treat incontinence. Further, Jamieson (1996) identified dyspareunia and pelvic pain in 46% and 39% of women as part of a clinical population of reproductive age women.

The causes of these pain symptoms are multiple, such as other medical conditions like interstitial cystitis, endometriosis, adhesions, scarring from other surgeries such as hysterectomies, dysmenorrhea, prior pelvic surgery, musculoskeletal dysfunction, estrogen status, and tissue pliability. The medical literature[39] and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline. Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction. Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth. Pelvic pain and other pain (inguinal and lower extremity related pain) is a known risk of sling procedures (or any other vaginal

[39] Norton (2014), van der Ploeg (2014)

surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures.

Of course, there are patients who have pelvic pain in addition to urinary incontinence and desire their incontinence treated. In the appropriate patient with urethral hypermobility and documented stress urinary incontinence, a TVT can be considered a first line treatment. Such patients may achieve a cure of their stress incontinence while their pelvic pain worsens. In my experience, this worsening of pelvic pain following TVT is unrelated to the TVT but rather is due to pelvic floor neural hypersensitivity. These patients with chronic pain and stress incontinence who desire a TVT (or another surgical treatment for incontinence) are warned about the possibility of worsening of pelvic pain after the anti-incontinence procedure. Studies have also shown that TVT has had a positive impact on sexual function.

Another potential complication of synthetic sling procedures is the risk of mesh exposure or erosion, which is an uncommon complication. An FDA review (2013) of MDRs between January 2008 and September 2011 showed that mesh exposures or erosions to occur at about 2%. The report goes on to say that most of the mesh exposures can be considered wound healing complications and can usually be treated very easily with conservative treatment, such as estrogen cream or a simple excision of the exposed mesh. The risk of erosion associated with sling procedures was well-known among pelvic floor surgeons even before TVT's release in 1998, as the medical literature reported on exposure and erosion in connection with prior synthetic slings. In addition, all pelvic floor surgeons understand from their training and experience that no treatment is guaranteed to cure SUI and complications can always occur. Rarely do synthetic MUS

need to be excised entirely. The risk of recurrent exposures is low as most exposures occur within the first year postoperatively. While mesh exposures are commonly referred to as "unique" complications associated with TVT and other mesh-based procedures, patients can also experience suture erosions or exposures from traditional repairs with both permanent and absorbable sutures.

I. 2011 AUA Survey of Mesh-Based Procedure Training

In 2011, the American Urological Association (AUA) conducted a survey of its members to determine how they learned how to perform mesh-based procedure training. They stated that in addition to readings from their core textbooks that they acquired their skills in the following modalities keeping in mind that each survey participant can select multiple sources for their learning. Among the survey participants, 48% learned from a company hands-on course, 32% were self-instructed, 26% took a company course without hands-on training, 23% learned these procedures in residency, 10% learned these procedures in fellowship, and 6% learned these procedures in a specialty society hands-on course.

J. TVT Professional Education Program Slide Deck (1998)

In 1998, Ethicon created a physician education slide deck to introduce physicians to TVT. The slide deck spoke about differences between traditional pubovaginal slings and the TVT procedure. The pubovaginal sling is a difficult operation with a complication rate approaching 25%. The pubovaginal sling is placed at the bladder neck and proximal urethra tension is applied to the sling. The TVT, on the other hand, is

a simple operation with a low complication rate with a sling placed at the mid urethra without any tension.

The slide deck describes the TVT as a piece of Prolene tape measuring 40 cm x 1.1 cm x 0.7 mm, loosely placed, without any elevation at the mid urethra. The slide deck clearly defined indications for the TVT, which include genuine stress incontinence, as well as a combination of stress and urge incontinence. The slide deck makes the important point that patients must be informed that the operation will only treat stress incontinence. When the TVT was first cleared in 1998, it was well-known, and also described in the IFU, that TVT was intended to treat stress urinary incontinence, and when performed on a patient that has mixed urinary incontinence, there may be a worsening of urge symptoms after the procedure. The slide deck makes note of key contraindications to the TVT, which include pregnant patients, patients with future growth potential, and women with plans for future pregnancy.

The slides mention that the mesh tape is encased in a protective plastic sheath, which remains in place until placement. The sheath, and the minimal dissection involved in its placement, minimizes the risk of infection of the tape. The slide deck is clear in the preoperative investigation of the patient that documentation of pure stress incontinence is indicated prior to selection of TVT as the procedure to be performed.

The slide deck counsels physicians about the potential risks and benefits of the procedure, which includes bleeding in the vagina or retropubic space, infection in the vagina or urinary tract, and injury to the bladder. Patients are prepared to stay overnight in the hospital, although most patients are discharged on the same day. Again, the slide deck reinforces the physician's awareness of these well-known complications. The slide

deck also mentions that the postmenopausal patient should have adequately estrogenized vaginal tissue. This point acknowledges that Ethicon was being proactive to make physicians aware that when incontinence procedures are performed in patients who are postmenopausal, they run the risk of urogenital atrophy which can lead to erosion of the mesh. Of further note is that this was mentioned and described in 1998 at the launch of TVT.

The slide deck discusses the concept of tensioning the sling, which ultimately is determined by the surgeons' judgment, similar to a pubovaginal sling. In fact, the slide deck refers to this as a "tension tests" that requires the patient to participate by coughing as the mesh was brought into its final position under the urethra. However, the slide deck recognizes that some patients will have this procedure performed under general anesthesia, and, in those cases, the surgeon must be comfortable leaving the mesh placed loosely around the mid urethra. The only measurement in this situation will be spacing with a blunt instrument. This statement makes physicians aware of the possibility that the mesh could be placed too tightly under the urethra resulting in voiding difficulties, which is a well-known potential complication of any incontinence surgery regardless of whether or not mesh is used.

The slide deck clearly describes the TVT procedure in terms of preparation, dissection, needle passage, and tape placement. Careful discussion of the abdominal and vaginal wall incisions are undertaken in the slide deck. It is recommended that the incision be 1 cm from the external urethral meatus and extended for only 1.5 cm along the course of the urethra. This incision is long enough to only accommodate the width of the TVT tape. A good description of introduction of the TVT device is made in the slide

deck. With one hand, a gentle grip is placed on the introducer. The needle tip is placed through the vaginal incision lateral to the urethra. The other hand is placed where the index or middle finger can be placed on the pelvic brim under the vaginal wall. In this manner, the curve of the TVT needle will rest in the palm of the hand as the needle is passed into the retropubic space. One is able to feel the needle passing behind the pubic bone and will pass lateral to the finger and the urethra.

The slide deck clearly mentions the risk of bladder perforation and vascular injury occurrence and it is noted to avoid perforation of the external iliac vessels by making sure not to be too lateral in the retropubic space. The potential for vascular and bladder injuries was discussed initially at the launch of TVT in 1998.

With regard to cystoscopy after passage of the needle, cystoscopy should be completed to verify bladder integrity. Cystoscopy should be repeated at the pass of the second needle as well. This is noted in the physician education slide deck. With regard to the tension tests, the slide deck is very clear on how they should be performed so as to minimize the risk of mesh contracture under the urethra. With the tension test, a scissors or hemostat is placed between the tape and the urethra. The abdominal ends of the TVT tape are pulled until there is contact between the tape and the instrument. The needles are separated from the tape while the plastic sheath is meant to remain in place, and the mesh is intended to lay flat. The tension test is completed with a full bladder, as the slide set makes clear. The TVT tape is adjusted with the patient coughing and then having the patient cough again. Once the procedure is completed with the mesh carefully placed under the urethra, the plastic sheath can be removed the tape can be cut. Next, the skin and the vaginal epithelium can be closed. The bladder can be emptied and the catheter

removed. The slide deck also mentions that after completion of the tension test, a Hegar dilator #7 or 8 should be able to be inserted through the urethra without any resistance. In other words, the tape should be neither palpable nor visible. In the postoperative period, Ethicon makes note of the possibility of bleeding and hematoma. For that reason patients are observed for such signs. The risks of urinary retention are also mentioned in the slide deck. Post-void residual should be obtained to make sure retention is not a possibility. In terms of follow up, the slide deck is very clear about how patient should be followed after mesh surgery. Patients should receive follow up appointments at 3 weeks, 6 months and yearly. The reason for annual follow-ups is because of the risk of complications, such as mesh erosion, mesh extrusion and or dyspareunia.

The slide deck is also clear to describe TVT complications. Perforation of the bladder is described in detail and this will be identified at cystoscopy. If bladder injury occurs, the TVT needle should be removed and replaced. An indwelling urinary catheter should also be placed. This should remain for several days and can be removed at the next office visit. The complication of vaginal bleeding and/or retropubic hematoma is also discussed in the slide deck. This can be managed conservatively with vaginal packing and may require percutaneous drainage. The slide deck describes the reasons for this stating that bleeding can occur but is usually limited by the retropubic space. These points show Ethicon's diligence in warning of these possible complications in their physician education programs.

The slide deck also provides some data regarding the pubovaginal sling using Prolene tape. Studies from Ulmsted, Wang, and Nillson are presented with 307 patients studied and a 2-year cure rate of 84%. The slide deck also described the early

complications of the Prolene tape procedure, which included voiding dysfunction ranging from 3-17%, UTI ranging from 3-6%, urge incontinence in 3% of patients, and miscellaneous complications such as wound infection and hematoma in a small number of patients. This physician education slide deck provided a very realistic overview of the procedure with the core complications that could occur as well as a suggested plan for how to handle them.

TVT Professional Education Program Manual (1998)

This is an extensive document provided to physicians interested in performing the TVT procedure. Contained in this guide is product information, package insert, warnings and precautions, adverse reactions, procedure overview, anesthesia, and clinical articles. Information is provided about the device, the TVT introducer, and information regarding the sterilization of the stainless steel instruments. A careful description of the TVT rigid catheter guide is provided. This guide is intended to facilitate the identification of the urethra and bladder neck during the surgical procedure. The guide is inserted into the Foley catheter positioned in the bladder via the urethra. This is an important step of the procedure and is emphasized well in this document.

The TVT instructions for use (IFU) is also provided in the Manual for all physicians to review. The instructions for use clearly states that this device should be used only by physicians trained in the surgical treatment of SUI. The instructions here are recommended for general use of the device. The instructions also state that variations in use may occur in specific procedures due to individual technique and patient anatomy.

The IFU is very clear about the indications for the TVT. The TVT device is intended to be used as a midurethral sling for treatment of female SUI resulting from urethral hypermobility or ISD. The TVT introducer and rigid catheter guide are available separately and intended to facilitate the placement of the TVT device.

The IFU describes in detail that this procedure can be undertaken under with either local, regional, or general anesthesia. Description about dissection, the use of the rigid catheter guide, the introducer, and placement of the TVT is provided in great detail. The instructions are very clear about how to pull the tape upward without tension under the mid urethra. The role of using patient feedback (for example, coughing with a full bladder) so that the tape can be adjusted appropriately is mentioned to physicians. The instructions clearly state to avoid tension of the tape, with the use of a blunt instrument such as scissors or forceps to be placed between the urethra and the tape during its removal. The instructions clearly state that premature removal of the sheath may make subsequent adjustments difficult.

The IFU clearly mention contraindications of this procedure. As with any suspension surgery, this procedure should not be performed in pregnant patients. Additionally, it is mentioned that polypropylene mesh will not stretch significantly. It should not be performed in patients with future growth potential including women with plans for future pregnancy.

The warnings and precautions of the device are discussed. TVT is not recommended to be used for patients on anticoagulation therapy and for those patients who have a UTI. The instructions clearly state that users should be familiar with surgical technique for bladder neck suspensions before employing the TVT device. It is, however,

important to recognize that TVT is different from a traditional sling procedure in that the tape should be placed without tension under the mid urethra. Of note, this is the second time the IFU mentions that physicians should be clearly knowledgeable about pelvic floor anatomy before they consider using this device. It is also the second time that mention is made that the mesh should not be on tension under the urethra. There is also discussion that cystoscopy should be performed to confirm bladder integrity or to recognize a bladder perforation. It is stated again not to remove the plastic sheath until appropriate tensioning has been determined. Again, it is mentioned that the tape is placed with minimal tension under the urethra. It is mentioned that the patient should be counseled that future pregnancies may negate the effects of the surgical procedure and the patient may again become incontinent. The instructions mention that should dysuria, bleeding, or other problems occur, the patient is instructed to contact their surgeon immediately. Again, this shows Ethicon's due diligence in warning physicians multiple times within the instructions for use of potential problems that can occur with implantation of the TVT device.

With regard to adverse reactions, the IFU mentions transient local irritation at the wound site and a transitory foreign body response may occur. This response could result in extrusion, erosion, fistula formation, and inflammation. Thus, Ethicon is warning physicians of the possibility of these problems that can occur as a result of the use of the TVT device. These problems are mentioned multiple times throughout this document so as to make physicians aware of their likelihood of occurrence. There is a discussion of overcorrection from the sling where too much tension applied to the tape can result in temporary or permanent lower urinary tract obstruction.

The IFU also discussed animal studies. It mentions that animal studies show the implantation of Prolene mesh elicits some minimal inflammatory reaction in tissues. This is transient and is followed by the deposition of a thin fibrous layer of tissue which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The material is not absorbed nor is it subject to degradation or weakening by the action of tissue enzymes when placed according to the guidelines in the IFU, Physician Education slides, and physician education documents.

The next section in the Manual is a procedure overview. First, there is a section on the Preoperative Investigation provided for the surgeon's reference. The indications for TVT are discussed. This includes genuine SUI. It is also mentions that a combination of stress and urge incontinence can be considered for TVT placement. However, the physician is warned to properly inform the patient that this operation will only treat the stress incontinence. It also mentions that this method allows definitive treatment for older women, overweight women, and patients who have undergone other operations for incontinence. The manual describes preoperative investigations to make sure the patient clearly has SUI. These investigations may include demonstration of urine leakage at stress test, and urine leakage during urodynamics procedures.

The next section of the Manual provides detailed information regarding the TVT surgical procedure. These details have been described above. A complete discussion of the postoperative care the patient is then undertaken. Pertinent points include the concept of urinary retention. The majority of patients return home without a catheter on the day of surgery. If the patient cannot empty the bladder completely when discharged following the procedure, the catheter may be left in place for three days. The patient

returns for repeat residual urine measurement, and, if it is not normal, she can be treated according to the local practice for postoperative urinary retention. Urinary retention is a well-known postoperative problem after any incontinence procedure. The Manual also describes the possibility of postoperative hematoma. These can occur in the abdominal and pelvic region. Bimanual palpation or ultrasound can also reveal the hematoma. If necessary, drainage can be performed if clinically indicated.

A discussion of bladder perforation is also undertaken. Perforation may be discovered with the TVT needle in situ during a routine cystoscopy carried out after each needle passage. If this occurs, the introducer and needle can be removed, and can be reintroduced somewhat more laterally. It is recommended to maintain close contact with the pubic bone. In this case the indwelling catheter should be left in place for several days and then removed. A discussion of infections is also undertaken in manual. It is noted here that wound infections seldom occur and they are usually the result of a poorly healed vaginal wall incisions. Polypropylene has been shown to produce little tissue reaction and does not itself predisposed to infection. (Falconer 2001). It is important for the physician to recognize that poor healing at the time of TVT surgery can result in mesh extrusion, typically at the wound site or incision line.

The next section of the manual talks about TVT patient education. There is a description about the normal anatomy of the pelvic structures. It also describes possible causes for SUI. A brief review of nonsurgical therapies is provided. A discussion of surgical techniques is mentioned including the needle suspension and the retropubic colposuspension. A discussion of sling procedures is also undertaken. A discussion of the TVT is described as an effective procedure for stress urinary incontinence. This will

create a new subcutaneous urethral backbone and was introduced initially in Scandinavia and Europe and then became available in the United States. At the time of this publication in 1998, approximately 5,000 patients had undergone TVT procedures. An 84% success rate was described. The majority of patients were released from the hospital on the same day without a catheter or any voiding problems.

K. Safety and Effectiveness of TVT and TVT-O

Based on my review of the medical literature and my professional experience, it is my opinion that the TVT's design is safe and provides both short-term and long-term effectiveness.

In my clinical experience, I have never had injury to any nerve, bowel, or bladder (other than incidental isolated recognized trocar injury to the bladder, easily treated with short-term catheter placement) during a TVT or TVT-O procedure. I have had three cases of TVT mesh extrusion, which were all treated with a simple in-office excision requiring only Metzenbaum scissors and forceps. None of the patients required surgical intervention, and no patient ultimately had their sling removed. No patient complained of long-term dyspareunia. My success rates are excellent and go out to 15 years with the use of TVT and TVT-O procedures, with most patients dry or significantly improved from baseline.

Synthetic slings are the most common type of surgical procedure performed today for SUI, and the monofilament, large-pore polypropylene used in TVT is the most common type of synthetic material used in slings. Slings have a number of advantages over the Burch colposuspension procedure. In that procedure, the vaginal wall is attached

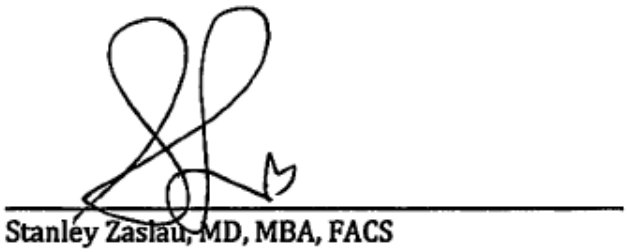
to the Cooper's ligament adjacent to the public bone. A longer hospital stay is required. Surgical times and recovery times are longer. Wound complications and hernia can occur. The laparoscopic Burch is less invasive but is more difficult to learn and perform, must be performed under general anesthesia, and requires multiple abdominal incisions. Cadaveric slings, another surgical treatment option, are rarely used for a number of reasons, including lack of durability and rejection issues.

Laser-cut versus mechanically cut mesh has become another topic of discussion for plaintiffs' experts. I have only had three patients with mesh extrusions over a 15-year period and could not determine a noticable difference between either mesh variation until I looked closely at the mesh with a magnifying glass. Personally, I have used both mechanically cut and laser cut TVT and TVT-O, and have not seen any difference in complication rates between either variation of mesh in my clinical practice or in the peer-reviewed medical literature. In the cases of urethrolysis I have performed over the years, I have not noticed or removed degraded particles of mesh, nor have I seen grossly altered structure of the knitting of the mesh in any of these specimens. Plaintiffs' experts' opinions related to the clinical implications or alleged roping, fraying, curling, degradation, particle loss, and cytotoxicity are unfounded and lack scientific reliability.

Conclusion:

The first-line, primary surgical treatment for SUI is the synthetic midurethral sling (including TVT or TVT-O) in West Virginia and throughout the world, due to their short learning curve, minimal morbidity, quicker return to normal activities and work, reduced operating and hospital times, and reduced use of anesthesia and pain medicine

compared to the traditional, abdominal procedures such as the Burch and autologous fascial slings. Although these older procedures remain within the standard of care, they are not the preferred first-line treatment option for uncomplicated surgical treatment of SUI. The benefits of synthetic midurethral slings outweigh the commonly known risks. The reproducibility and favorable safety profile of the TVT and TVT-O have established synthetic midurethral slings as the benchmark anti-incontinence procedure and preferred treatment option for surgeons and patients throughout the world.



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DATE: January 13, 2017